

## **REMARKS**

Claims 29-34 are currently pending in the application. Claims 31 and 32 have been canceled. Claim 29 has been amended to more particularly point out and distinctly and clearly claim the invention. The amendments are made without prejudice, do not present any new matter, and are not made to overcome any prior art rejection.

Claims 29-34 are rejected under 35 USC §112. The Office Action alleges that in claim 29, it is unclear (from the specification) whether the cut-off of 9 for the optical density (OD) is dependent on the particular assay/equipment used.

In response thereto, Applicants submit that optical density is a fairly routine measurement that can readily be carried out by one skilled in the art, and the claims should not be limited to a specific assay or equipment type in order to specifically point out and claim the invention. Accordingly, it would be inappropriate to require amendment of the claims in this fashion, and would simply invite infringement by third parties. One skilled in the art can readily determine optical density using a variety of techniques and skills known in the art.

Claims 29, 31 and 33 are rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over U.S. Patent No. 5,770,195 (“Hudziak”) in view of Esteva, in view of Pinkas-Kramarski, and further in view of Hoffmann. Applicants respectfully traverse the rejection.

Applicants have amended claim 29 to recite detecting not only HER3, but additionally assaying for one or more of HER1 (EGFR), pHER1, HER2/neu, and pERK in cells.

None of the cited references, either alone or in combination, teach or suggest the instantly claimed methods in view of the above. Hudziak does not disclose the existence of HER3, much less its use as a biomarker. Esteva fails to disclose or suggest that any of the biomarker patterns of expression could be used to select a subject for treatment with a molecule targeting EGFR.

Applicants also note that Pinkas-Kramarski does not teach or suggest treatment with any therapy, much less a therapy based on anti-EGFR antibody as required by the present claims.

The deficiencies of Hudziak, Esteva and Pinkas-Kramarski cannot overcome by combination with Hoffmann. Hoffman relates to expression of receptors (such as ErbB-2 and ErbB-3) and how they are associated with TNF- $\alpha$  insensitivity. Hoffman noted that TNF- $\alpha$  resistance was based on either the expression of EGFR or the expression of both ErbB2 and ErbB3 (HER-2 and HER-3).

In view of all of these references, one skilled in the art -- even with this combination of references -- would not have been motivated to arrive at the instant invention. All of claim limitations are neither taught nor suggested by the combination of Hudziak, Esteva Pinkas-Kramarski and Hoffmann. Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 29-34 are also rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over Hudziak in view of Esteva, in view of Pinkas-Kramarski, in view of Hoffmann, and further in view of Yang *et al.*, *Critical Reviews on Oncology/Hematology*, 38: 17-23 (2001) (“Yang”). This rejection is traversed.

Yang simply adds recitation of the ABX-303 antibody. Yang’s combination with Hudziak, Esteva, Pinkas-Kramarski and Hoffmann (discussed above) does not even suggest let alone render obvious all of the claim limitations, as amended. Applicants therefore respectfully request reconsideration and withdrawal of the rejection.

## **CONCLUSION**

Based on the above, Applicants believe the claims are now allowable. If there are any questions or comments regarding this response, the please contact the undersigned attorney at 805-447-4128.

Respectfully submitted,

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